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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/606,976	06/25/2003	Daniel G. Stearns	XENOP009	6444

58766 7590 08/04/2008

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EXAMINER	
GUPTA, VANI	

ART UNIT	PAPER NUMBER
3768	

MAIL DATE	DELIVERY MODE
08/04/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)
	10/606,976	STEARNS ET AL.
	Examiner	Art Unit
	VANI GUPTA	3768

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.
2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.
3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-52* is/are pending in the application.
4a) Of the above claim(s) _____ is/are withdrawn from consideration.
5)☐ Claim(s) _____ is/are allowed.
6)☒ Claim(s) *1-52* is/are rejected.
7)☐ Claim(s) _____ is/are objected to.
8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.
10)☒ The drawing(s) filed on *25 June 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a)☐ All b)☐ Some * c)☐ None of:
1.☐ Certified copies of the priority documents have been received.
2.☐ Certified copies of the priority documents have been received in Application No. _____.
3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date
3/11/08;1/23/08;8/28/07;4/20/07;1/08/07;10/16/06;2/13/06;9/12/05;7/27/05;11/26/04;1/05/04;.
4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claim Rejections - 35 USC § 101

1. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

1. ***Claims* 1- 40** *are rejected under 35 U.S.C. 101 because the claimed inventions are directed to non-statutory subject matter.*

Regarding **Claim 1,** the claim language does not include a sufficient tie to an apparatus; i.e., these steps can be accomplished by hand. Dependent **Claims 2 – 40** merely add further details of the calculations recited in Claim 1 without including any tie to another statutory category.

In order for a method to be considered a "process" under §101, a claimed process must either: (1) be tied to another statutory class (such as a particular apparatus) and (2) transform underlying subject matter (such as an article or materials). See Diamond v. Diehr, 450 U.S. 175, 184 (1981); Parker v. Flook, 437 U.S. 584, 588 n.9 (1978); Gottschalk v. Benson, 409 U.S. 63, 70 (1972). If these requirements are not met by the claim, the method is not a patent eligible process under §101 and is non-statutory subject matter.

Therefore, Claims 1 - 40 also fall under judicial exception as abstract ideas; i.e., the method and does not specifically claim to transform one physical entity into another entity.

Additionally, these claims also do not specifically claim achieving "useful, concrete and tangible results," because they do not provide the following: (1) that the utility of the invention is specific, substantial, and credible; (2) a practical application, or "real-world" results; (3) and a

result that can be assured or substantially repeatable, and the process can not substantially produce the same result again.

Claim Rejections - 35 USC § 102

1. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

2. ***Claims 41 – 52*** *are rejected under 35 U.S.C. 102(e) as being anticipated by Nilson et al. (US 6,615,063 B1).*

Regarding **Claims 41 – 52,** Nilson presents an imaging system, comprising a light-tight imaging box (fig. 1, #12) configured as a set of walls enclosing an interior cavity. The imaging system also includes a camera mount configured to position a CCD camera relative to a fixed datum on one of the walls for viewing by the camera and a light transmission device. The imaging system additionally comprises a moveable stage apparatus including a transport mechanism and a stage configured to support the sample within the interior cavity. The stage is coupled to the transport mechanism for movement of the sample to one of a plurality of positions in the interior cavity. The transport mechanism and the light transmission device cooperate to direct light reflected or emitted from the sample to the fixed datum to capture the image by the camera (col. 1, lines 1 – 15; col. 4, lines 13 – 30).

With further respect to **Claims 48 – 52**, Nilson discloses that the image processing unit can interface between the camera and a standard computer (fig. 1A, #28) that comprises the usual components such as a processor, memory components such as random-access memory (RAM) and read-only memory (ROM), and disk drive components (e.g., hard drive, CD, floppy drive, etc.). These components make it possible for one to load and execute the program instruction stored on a computer readable medium such a floppy disk or compact disc (col. 1, lines 44 – 54).

Like all standard computers, Nilson's computer also comprises a display (#38); input devices such as a keyboard (#40) and mouse (#42); communication ports to connect to and communicate with various components in the imaging box; and processing hardware and software configured to provide output for controlling any of the devices in the imaging box, including the camera; and the graphical user interface (GUI)-based display or monitor (#38) for presenting imaging information to the user(col. 1, lines 51 – 67).

All these components make it possible for the computer to perform the aforementioned steps of the present invention, such as producing structured light representations using 2-D structured light images taken from one or more positions of the stage in the interior cavity (col. 2, lines 18 – 21).

Photon emission data may represent the specific pixels on the CCD camera that detect photons over the length of the image-capture period. Together, the structured light photographic representation of the sample and a luminescence representation of the sample may be combined to form a structured light superposition or overlay image. Because the imaging apparatus is typically used to measure the entire sample, the data in the luminescence representation generally

has one or more distinct luminescent portions of interest. One can overlay the luminescent image with ae photographic image and display the two images together as a 2-D "overlay" image, with the luminescence data typically shown in pseudo-color to show intensity. Multiple luminescence representations may be taken from the same position of stage, e.g., at the same time or a later time. Additionally, a 3-D luminescence image may be generated by collecting emitted photons received by each detector pixel of the CCD camera over a defined length of time. In other words, the luminescence image may display magnitude values representing the photon counts at the individual detector pixels; and sections of the sample emitting radiation (e.g., photons) will show in the luminescence image (col. 15, lines 41 – 55).

Claim Rejections - 35 USC § 103

3. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

4. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

5. **Claims 1- 40** are rejected under 35 USC 103(a) as being obvious over *Nilson et al. (US 6,615,063 B1)* in view of Ntziachristos et al. (6,615,063 B1), further view of Bruder et al. (7,263,157 B2).

Regarding **Claims 1 – 40**, Nilson explains that specialized in-vivo imaging applications is an analysis of one or more representations of photon emissions from internal portions of a specimen superimposed on a photographic representation of the specimen. In-vivo imaging is performed by capturing an image of the sample using an intensified or cooled charge-coupled device (CCD) camera to detect the localization of low intensity light-producing cells (e.g. certain bacteria or tumor cells made bioluminescent by transforming them with luciferase DNA constructs) in a living animal such as a mouse (col. 1, lines 5 – 45).

Nilson also explains how it is possible to produce in-vivo images for analysis of one or more representations of emissions from internal portions of a specimen superimposed on a photographic representation of the specimen. An imaging system is comprising a low intensity light source, such as luminescence from luciferase-expressing cells, fluorescence from fluorescing molecules, etc., allows 2-D and structured light imaging. The low intensity light source may be discharged from any of a variety of light-emitting objects or samples, and animals or plants containing light-emitting molecules, such as mice containing luciferase expressing cells. It is also possible to acquire photographic or reflection-based images of a sample or animal. Additionally, a 2-D luminescence image may represent a collection of emitted photons received by each detector pixel of the CCD camera over a defined length of time. In other words, the luminescence image may display magnitude values representing the photon counts at

the individual detector pixels; and sections of the sample emitting radiation (e.g., photons) will show in the luminescence image (col. 1 line 53 – col. 2, line 67) .

Nilson's method for capturing images of the mouse is based on light emitted by the mouse. Photon emission data may represent the specific pixels on the CCD camera that detect photons over the length of the image-capture period. Together, a structured light photographic representation of the sample and a luminescence representation of the sample may be combined to form a structured light superposition or overlay image (col. 15, line 41 – col. 16, line 19).

The mouse is supported by a stage moveable (Fig. 3A and 3B) within an imaging box that is coupled to a camera configured to capture an image of the mouse resting on a stage within the box. The method includes moving the stage to a first position in the imaging box; capturing a first image of the sample from the first position using the camera; and moving the stage to a second position in the imaging box. The second position has a different angle relative to a fixed datum associated with the camera from the first position. Additionally, a second image of the mouse from the second position may be acquired by the camera (col. 2, lines 36 – 49).

As explained above, images of the animal may be acquired from different views, angles, and positions within the imaging box. These images may be used in in-vivo imaging applications that include analysis of one or more representations of emissions from internal portions of the mouse superimposed on a photographic representation of the same mouse. For each of the positions, one or more photographic and/or luminescence images of the sample may be acquired. Multiple luminescence representations may be taken from the same position of stage, e.g., at the same time or a later time. Additionally, the luminescence is recorded as a function of position to produce the luminescence image. Image collection may also be accomplished by capturing

images of the sample from alternate positions and views of the sample (col. 4, line 1 – col. 5, line 67).

Since one is considering the animal as a whole, the data in the luminescence representation generally has one or more distinct luminescent portions of interest. One can overlay the luminescent image with the photographic image and display the two images together as a 2-D overlay image, with the luminescence data typically shown in pseudo-color to show intensity. After the 2-D structured light images have been captured and stored, a computer connected to the imaging system processes the structured light data to produce a structured light representation. This structured light projection system allows one to obtain 3D surface topology (col. 15, line 41 – col. 16, line 19).

However, each structured light image provides surface topology for approximately half of the animal, only. Nilson compensates for this shortcoming by taking images from several viewing angles, or about every 45 degrees. Thus, the entire 3D surface of the mouse can be reconstructed by "attaching" the partial surface reconstruction generated from each view.

Nilson differs from Claim 1 - 40 in that he does not appear to specifically disclose creating a set of volume elements. In addition, Nilson does not specifically disclose varying the number of volume elements and varying the configuration of volume elements, to produce a set of solutions for the three-dimensional representation of the source distribution; or that these variations involve adaptive meshing.

However, Ntziachristos teaches fluorescence-mediated molecular tomography, wherein diffraction tomography segments the volume under investigation into a number of discrete voxels, or volume elements, into a “mesh” (col. 10, line 34 - col. 11, line 18).

Ntziachristos also presents a cost-efficient embodiment of his invention, with which one can collect bulk information, using economical, massively parallel continuous-wave measurements (~1000 channels); and highly specific information of absorption and scattering parameters, using smaller array of time-domain source-detection channels (~50 – 100 channels) (col. 12, lines 6 – 30).

Accordingly, Ntziachristos complements the disclosing of Nilson by teaching an invention that enables three-dimensional localization in deep tissues and quantization of molecular probes (Abstract).

Ntziachristos does not specifically disclose details a cost function that is useful in optimizing the retrieval or measurement of surface photon density.

However, Bruder teaches the use of a cost function that is a sum of weighted addends. Each addend can be formed from the difference of a measurement value associated with the detector and a mapping function, the mapping function describing the connection between a theoretical measurement value of the reference position of the reference object mapped in the detector dependent on the reference position, the geometry of both acquisition systems, the rotation angle position and the system angle to be optimized. The specification of the mapping function preferably results in the form of fan geometry coordinates (col. 2, line 41 through col. 3, line 30).

Based on the mapping function, a cost function can be formed and minimized or optimized such that reference position(s) of a reference object and system angles can be determined. The optimization of the cost function can be achieved by standard methods that are commonly known; such as the Simplex Method, and other algorithms or optimization methods,

utilizing linear ordinary differential equations (for example, Green's function and Finite Element Modeling) (col. 3, lines 50 – col. 7, line 3).

Accordingly, Bruder complements Nilson and Ntziachristos by teaching a tomography apparatus with at least two acquisition systems are respectively each disposed in the azimuthal direction at respective specific system angles around a common rotation axis. This enables artifact-free reconstruction of a slice or volume image using the system angles determined in this manner (abstract).

*Therefore, it would have been prima facie obvious to combine Nilson with the teachings of Ntziachristos and Bruder to obtain the invention in the instant **Claims 1 – 40**.*

Conclusion

6. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

a. Potter (US 5,205,291) for in-vivo fluorescence photometer; and

b. Sevick-Muraca et al. (US 5,865,754) for fluorescence imaging system and method.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to VANI GUPTA whose telephone number is (571)270-5042. The examiner can normally be reached on Monday - Thursday; 7:30 - 6:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brian Casler can be reached on 571-272-4956. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Brian L Casler/
Supervisory Patent Examiner, Art Unit 3737

/Vani Gupta/
Examiner, Art Unit 3768